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Hospital based study of prognostic factor of endometrial cancer patients

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Abstract

Background: Endometrial cancer (EC) is the sixth most common cancer in women worldwide (fourteenth most common cancer overall), with 320,000 new cases diagnosed in 2012 [1]. The declining trend of cervical cancer and the predicted rise of endometrial cancer in India means that endometrial cancer will be a significant issue in India. We studied and analyzed the demographics, staging, treatment details, and outcomes of operated cases of endometrial cancers.

Material and Methods: This is a retrospective study carried out at IGIMS, from 2008 to 2017. All patients of histopathologically proven endometrial cancer operated in the department during this period were studied and analysed. **Results:** In our study we found 46 EC patients with a median age of 58 years (40-70 years). 41 patients had postmenopausal bleeding and rest 5 had complains of discharge per vagina. 41 patients were found to have lesion limited to less than half of myometrium and no lymph node involvement and so were not given any adjuvant therapy. 5 patients required adjuvant therapy following surgery. The pathological stages were Stage IA in 28 patients, Stage IB in 10 patients, Stage II in 4 patients, Stage IIIC1 in 3 patients, Stage IIIC2 in 1 patient. Grade 1 tumor were seen in 23 patients, Grade 2 in 13 patients, and Grade 3 in 10 patients. With a median follow up of 5 year OS was 86.84%. Age >60 years, Stage III or greater, and non endometrioid adenocarcinoma were independent prognostic factors that adversely affected overall survival (OS). **Conclusions:** Prognosis of patients with endometrial cancer is good as they become symptomatic in early stage and hence are diagnosed and treated early as compare to ovarian and cervical cancer. However, elderly status, higher stage, and a poorly differentiated tumor are associated with poor outcomes in endometrial cancer.

Keywords: Endometrial cancer, hysterectomy, postmenopausal, postmenopausal bleeding, prognosis, survival

Introduction

Endometrial cancer is the most common gynecological malignancy in developed countries. It is estimated that 61,380 new uterine cancer cases will occur in 2017, with 10,920 death resulting from the disease (US) [1]. In India endometrial cancer is the 9th most common cancer among women and 3rd most common gynaecological cancer with 12325 new cases and age-standardised incidence rate of 2.3 and mortality rate of 0.9 according to Globocon 2012 [2]. With the changing life style and increasing incidence of diabetes, hypertension and obesity the incidence of endometrial cancer is increasing and is projected to soon become a major health burden even in the developing countries.

Majority (70%) of endometrial cancers are diagnosed with localized disease and have a favourable 5-year survival of 95%. The median age at diagnosis has been reported to be around 62 years. The risk factors proposed to be contributing to this cancer are obesity, diabetes, hypertension, endogenous or exogenous estrogen, nulliparity, menopause, family history, and endometrial hyperplasia. With the advent of better surgical techniques radiotherapy and chemotherapy, the mortality rates of endometrial cancer are declining.

The work up and treatment of endometrial cancer entails surgical staging according to criteria established by the International Federation of Obstetrics and Gynecology (FIGO), which includes a total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO), and pelvic/para-aortic lymph node dissection (LND), withomentary biopsy and pelvic washings. Depending upon the patient's risk factor for recurrence management and adjuvant treatment after surgery are decided. Adjuvant therapies include vaginal vault brachytherapy (VBT), pelvic external-beam radiation therapy (EBRT), and/or chemotherapy (CT). The risk factor considered for decision of adjuvant therapy are age, grade, histologic type, deep of myometrial invasion,

tumor extension, tumor extension beyond the uterus, and lymphovascular space invasion. Depending of these risk factors, patients are grouped into low, intermediate or high risk for recurrence and most debate and controversy is associated with the patients stratified to the intermediate-risk group [3]. As a result, variability in the management of endometrial cancer across centers is common. This variability may have an impact on outcomes.

Pathologically it is divided into two type, malignant epithelial tumor (pure endometroid cancer, uterine serous carcinoma, clear cell carcinoma, carcinosarcoma and undifferentiated / dedifferentiated carcinoma) and stromal or mesenchymaltumor types (uterine leiomyosarcoma, endometrial stromal sarcoma, undifferentiated uterine sarcoma adenosarcoma, and perivascular epithelioid cell neoplasm) [4, 5, 6]. Depending on the etiology EC divided into two types – type I (estrogen dependent) and type II (estrogen independent). Overall morbidity and mortality of endometrial cancer is low because most patients present at early stage because of abnormal bleeding [7]. Incidence of endometrial cancer is increasing due to increase in life expectancy and increasing incidence of hypertension, obesity, hypothyroidism and diabetes mellitus [8-10]. So, it will become a significant issue in coming year.

However, there is limited literature about the prognosis and practices in the management of endometrial cancer available

from India. Lack of such information hampers the development of strategies to improve the outcome and prognosis. The aims of this study was to evaluate the prognostic factor which effects the outcome of treated endometrial cancer patients

Material and methods

This retrospective study was done in IGIMS from 2008 to 2017 after ethical approval. 52cases of endometrial cancer were operated during these 10 years. The patients’ files were retrieved from the medical record section and their clinical history and associated risk factors were evaluated. All patients were tried to be contacted and followed up. 46 of these patients were included in the study as the files of 2 patients could not be retrieved and 4 patients could not be contacted. The case records of these patients were reviewed which included detail of surgery notes, pathology reports, and physical examination notes. Age, menopausal state, parity, date and type of operation, histopathological diagnosis and stage; size, location and grade of tumor; state of myometrial and lymphovascular invasion (LVI), the presence of nodal involvement; type, duration and dose of therapy; location and occurrence of recurrences and metastases; last follow-up date and present status were recorded.

Result

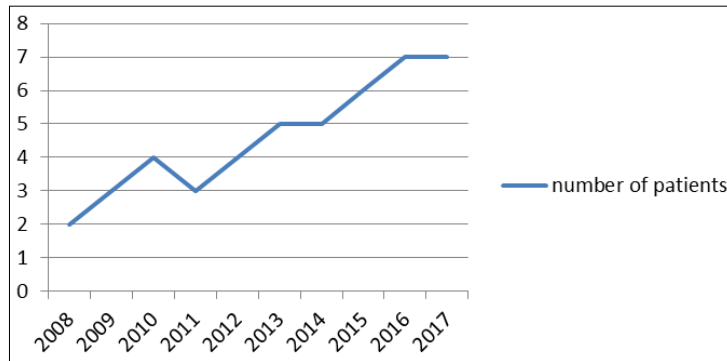


Fig 1: number of cases of endometrial cancer operated yearly.

Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number of patients	2	3	4	3	4	5	5	6	7	7

Table 1: Distribution of EC patients according to their age.

Age group(year)	41-50	51-60	>60
Number of patients(percentage)	2	12	32

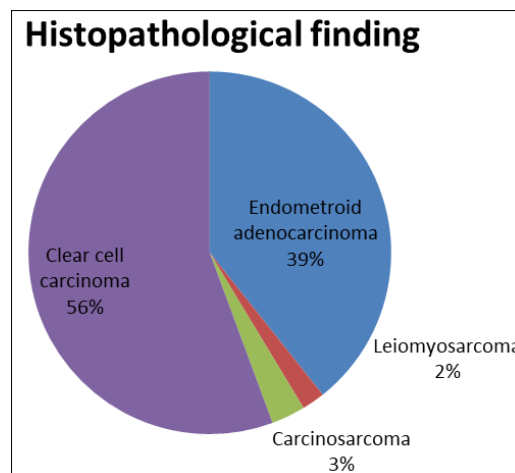


Fig 2: Distribution of EC patients according to histopathology.

Histopathological finding	Number of patients	Percentage
Endometroid adenocarcinoma	39	84.78%
Leiomyosarcoma	2	4.43%
Carcinosarcoma	3	6.52%
Clear cell carcinoma EC	2	4.43%

Table 2: Treatment given and Follow up analysis of EC patient

Treatment given		EC (n=46)		Percentage			
Surgery		41		89.13%			
Chemotherapy given		5		10.87%			
Follow up analysis (Survival)		EC (n =46)		Histopathology		Staging	
		Age >60years	Age< 60 years				
Survival >5years	Disease free	14(46.67%)	16(53.33%)	Endometroid adenocarcinoma 30		Stage IA	
	Recurrence	2(66.67%)	1(33.33%)	Carcinosarcoma 1		Stage IB	
				Clear cell carcinoma 1			
Survival < 5years		4(80%)	1(20%)	Endometroid adenocarcinoma 1		Stage IIB	
Loss to follow up		6	2	Carcinosarcoma 2		Stage IIIC1	
				Clear cell carcinoma EC 1		Stage II	
				Leiomyosarcoma2		Stage IB	
				Endometroid adenocarcinoma 8		Stage IA	

In the last 10 years there was increasing trend of EC. 46 patients were operated for EC. Median age of these patient was 59 years, ranging between 41 and 75. There were 14 patients under age of 60 and 32 were over the age of 60 figure 1 and table 1. 40 patients had postmenopausal bleeding and rest 6 had abnormal pus discharge per vagina. Median parity was 3 (0-5) with 2 nulliparous, 6 primiparous and 38 multiparous patients. The histopathological finding, staging, treatments given and patient's outcomes are shown in figure 2 and table 2. Most of cases were endometroid adenocarcinoma (39 patients, 84.78%). 41 patients had less than 1/2th of myometrial invasion histologically and no lymph node invasion so, treated only by type I hysterectomy and pelvic lymph node dissection only. Rest 5 EC patients had more than 1/2 of myometrial invasion or lymph node invasion and hence given adjuvant in the form of radiotherapy alone or chemo radiation. The pathological stages were Stage IA in 28 patients, Stage IB in 10 patients, Stage II in 4 patients, Stage IIIC1 in 3 patients, Stage IIIC2 in 1 patients. With a median follow up of 5 year OS was 86.84%. Age >60 years, Stage III or greater, and non endometroid adenocarcinoma were independent prognostic factors that adversely affected overall survival (OS).

Discussion

The present study was done to evaluate the prognostic factors that affect the outcome of endometrial cancer patients who were operated in our Institute from 2008-2017. 46 patients were eligible for the study. An attempt has been made to study the factors, clinical finding, surgical staging and histopathological type that can influence the survival.

The 5-year overall survival (OS) rate for the entire population was 77% (stages I-IV) has been reported in a study [11]. A study was conducted in Norway to investigate how changes in therapeutic strategies during a 30-year period are reflected in survival changes through careful characterization of a population-based series of 1077 endometrial carcinoma patients [12]. There was an increase in number of patients of endometrial cancer, the number of patients treated rose from 286 (1981-1990) through 307 (1991-2000) to 484 (2001-2010). Main treatment changes included increase in adjuvant chemotherapy from 0% through 3-9% and a dramatic reduction in adjuvant radiotherapy from 75% through 48-12% (all p<0.001). 5-year disease-specific survival increased significantly during this 30-

year period, from 75.8 through 80.2-86.9% (p=0.002) and overall survival from 67.8 through 71.7 to 77.8% (p=0.03) [12]. In our study, the 5-year OS was 86.84% which is comparable to the above studies.

Age is known to be an important factor that determines the prognosis. In a retrospective review of 263 patients conducted to assess the relationship between selected clinical and pathological factors and disease free survival (DFS) and overall survival (OS) in endometroid endometrial cancer patients, it was observed that the worse OS was related to younger age at menopause (HR=0.932; 95%CI=0.873-0.996; p=0.0039) [13]. A moderate age gradient was observed, with 5-year relative survival decreasing from 90% in the age group 15-49 years to 75% in the age group of beyond 70 years [14, 15]. In our study, we found that the five-year survival rates for younger patients (≤60 years) was better than the older patients.

The results from various studies suggest that history of obesity and diabetes may increase risk of mortality after endometrial cancer diagnosis; modification of these characteristics may improve survival even after endometrial cancer diagnosis [16, 17]. In an earlier study, it was found that survival for >5 years was 82% for women without hypertension and 72% for women with hypertension in a set of endometrial cancer patients. [18] Our study also showed better outcome for those with no adverse family history, hypertension and diabetes mellitus (not mentioned in table).

Over the years, effective treatment has been offered which has translated into better survival rates for patients of endometrial cancer. Surgically-treated EC patients, treated either by surgery alone or in combination with other treatment modalities (radiotherapy or chemo radiotherapy) depending on the histology and surgical staging, showed better five-year survival rates [19]. In 2017 according to NCCN guideline the adjuvant therapy is given for patients with stage IA, grade 3 disease with additional risk factors and stage IB grade 3 disease without adverse risk factors [20].

The present study on endometrial cancer survival, has shown that age at diagnosis, extent of disease, family history, diabetes, hypertension and treatment are important determinants for prognosis. It can be concluded that the current study showed that younger patients (≤50 years), with no history of diabetes, hypertension, family history of cancer, non-tobacco user, and those diagnosed with localized-disease, treated with surgery,

either alone or in combination had better survival than their respective counterparts. Further more detailed clinical study will be helpful in understanding the prognostic indicators for survival especially with the newer treatment technologies available now.

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